

**BROOKHAVEN NATIONAL LABORATORY**

**BIOLOGY DEPARTMENT**

# **BNL-3 RUN**

## **FINAL REPORT**

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## **TABLE OF CONTENTS**

Executive Summary	3
Participants	4
Participants Statistics	6
Beam Characteristics	7
Run Dates	8
Beam Time Description	8
Experimenters and Run Statistics	9
Experimenters and Biological Samples	10

## EXECUTIVE SUMMARY

During the Fall of 1997, a series of radiobiological and physics experiments were performed using the BNL's Alternating Gradient Synchrotron (Experiment 919, BNL-3). These experiments were part of NASA's Space Radiation Health Program (SRHP), heavy ion radiobiology research program at BNL.

A total of 22 groups participated in the BNL-3 run, 16 of which were returnees from 1996's BNL-2. Six groups were new participants. From the total number of participants, 20 groups were full proposals and 3 were piggyback experiments. These represented 21 institutions from United States, and 1 from Japan, totaling 64 users. Their experiments were dedicated to the study of the physics characteristics and the biological effects of  $^{56}\text{Fe}$  ion beams on detectors, and a hierarchy of biological systems ranging from isolated DNA, to cells, tissues and animals. A total of 1800+ biological samples were irradiated at the AGS A-3 beam line, employing 82 hours of beam time. In addition, 37 hours were used for physics experiments, and a total of 30 hours were necessary for beam characterization, dosimetry, and calibration.

During the BNL-3, AGS provided iron beams with two energies: 1 GeV/nucleon (1.06 GeV/nucleon\*, LET: 148 keV/ $\mu\text{m}$ ), and 0.6 GeV/nucleon (0.565 GeV/nucleon\*, LET: 177 keV/ $\mu\text{m}$ ) for biology and physics experiments. The dose/rates used were as low as 7 cGy/min and as high as 16 Gy/min for 1 GeV/nucleon, and from 10 cGy/min up to 16 Gy/min for 0.6 GeV/nucleon iron beams. The spill rate employed was 30 spills/min with a duration of 500 msec/spill. The spill fluence was (particles/spill)  $3.9 \times 10^8$  (max) and  $2.1 \times 10^6$  (min) for 0.6 GeV/nucleon; and  $4 \times 10^8$  (max) and  $1.7 \times 10^3$  (min) for 1 GeV/nucleon. The intensities (particles/ $\text{cm}^2/\text{sec}$  on target) used during the run were  $1.12 \times 10^7$  (max) and  $5.97 \times 10^3$  (min) for 0.6 GeV/nucleon,  $1.12 \times 10^7$  (max) and  $4.92 \times 10^5$  (min) for 1 GeV/nucleon. A 7.5-cm diameter beam spot was employed for the exposures.

One of the highlights from BNL-3 was the use for the first time of a robotic sampler changer provided by the National Institute of Radiological Sciences from Japan. The device was employed by 3 groups, and demonstrated the advantages of having such a device for the exposure and exchange of samples under different operational conditions. In general, all the users were able to complete their experimental protocols. However, in one case, a set of samples was exposed incorrectly due to problems in the beam control operations, jeopardizing the interpretation of the results. After the run, the failure was identified and appropriate measures were taken to avoid similar incidents.

Radiobiological experiments employed cells, tissues and intact specimens, which required a complex coordination and planning of their respective logistic support. Biological studies used human, mouse, rat, hamster and canine cell lines (25), human-hamster hybrid cell lines, chick neural tissue (retina) and intact specimens (rodents). The full program was completed in 8 days (180 hours) under the AGS's operation schedule and with the allocated beam time dedicated for the NASA radiobiology program.

\* Actual beam energy on target

# PARTICIPANTS

<b>Exp.</b>	<b>Participants</b>	<b>Affiliation</b>	<b>Title</b>
B-1	J. Miller L. Heilbron C. Zeitlin R.P. Sigh K. Holabird M. Nyman W. Holley W. Schimmerling	Lawrence Berkeley National Laboratory, CA " " " " " " " NASA, HDQ, Washington DC	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker Ph.D., Co-Worker
B-2	D. Chen T. Hei	Los Alamos National Laboratory, NM Columbia University, NY	Ph.D., Principal Investigator Ph.D., Co-W
B-3	T.C. Yang S. Yamada P. Riggs H. Wu K. George	NASA, Johnson Space Flight Center, TX " " Kelsey-Seybold Co., TX KRUG, TX	Ph.D., Principal Investigator Co-Worker Co-Worker Co-Worker Co-Worker
B-7	B. Rabin J. Joseph B. Shukitt-Hale J. McEwen	University of Maryland Baltimore County, MD " " "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Investigator Tech. Support
B-9	B. Sutherland P. Bennett J. Sutherland J. Trunk D. Monteleone N. Metting	Brookhaven National Laboratory, NY " " " " Pacific Northwest National Laboratory, WA	Ph.D., Principal Investigator MS., Biology Associate Ph.D., Co-Worker Co-Worker Co-Worker Ph.D., Co-Worker
B-10	L. Lutze-Mann R. Winegar P. Chang	University of California, CA SRI International, CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Ph.D., Co-Worker
B-12	T. Hei C. Piao R. Miller	Columbia University, NY " "	Ph.D., Principal Investigator Co-Worker Co-Worker
B-13	E. B-Kubiczek G. Harrison	University of Maryland, MD "	Ph.D., Principal Investigator Ph.D. Co-Worker
B-14	N. Metting B. Sutherland	Pacific Northwest National Laboratory, WA Brookhaven National Laboratory, NY	Ph.D., Principal Investigator Ph.D., Co-Investigator
B-15	C. Waldren M. Lenarczyk T. Hei	Colorado State University, CO " Columbia University, NY	Ph.D., Principal Investigator Co-Investigator Ph.D., Co-Investigator
B-18	P. Cooper B. Rydberg E. Kwoh	Lawrence Berkeley National Laboratory, CA " "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Co-Investigator
B-19	A. Kronenberg C. Wiese S. Gauny	Lawrence Berkeley National Laboratory, CA " "	Ph.D., Principal Investigator Post-Doctoral Student Senior Research Associate
B-20	A. Kronenberg A. Grosovsky C. Wiese S. Gauny	Lawrence Berkeley National Laboratory, CA University of California Riverside, CA Lawrence Berkeley National Laboratory, CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator Post-Doctoral Student Senior Research Associate
B21	G. Nelson G. Kasarian W. Schubert	Loma Linda University, CA " "	Ph.D., Principal Investigator Co-Worker Co-Worker
B22	M. Vazquez J. Miller	Brookhaven national Laboratory, NY Lawrence Berkeley National Laboratory, CA	MD, Ph.D., Principal Investigator Ph.D., Co-Principal Investigator

<b>Exp.</b>	<b>Participants</b>	<b>Institution</b>	<b>Title</b>
B-23	A. Brooks S. Bao K. Rithidech	Washington State University, WA " SUNY, Stony Brook, NY	Ph.D., Principal Investigator Co-Worker Ph.D., Co-Worker
B-24	T. Borak B. Gersey	Colorado State University, CO "	Ph.D., Principal Investigator Student, Co-Worker
B-25	H. Evans T. Evans	Case Western Reserve University, OH "	Ph.D., Principal Investigator Assistant
B-26	W. Morgan C. Limoli	University of California, CA "	Ph.D., Principal Investigator Ph.D., Co-Principal Investigator
B27	T. Jorgensen P. Russell M. Moskovitch	Georgetown University Medical C., DC " "	Ph.D., Principal Investigator Research Associate Ph.D., Co-Worker
B28 (* )	Y. Furusawa M. Matsufuji M. Saito	National Institute of Radiological Sciences, Japan " "	Ph.D., Principal Investigator Ph.D., Co-Worker Student Co-Worker
B29 (* )	N. Mohan	The University of Texas Health Sciences at San Antonio, TX	Ph.D., Principal Investigator
B-30 (* )	P. Kale	Alabama Agricultural and Mechanical U., AL	Ph.D., Principal Investigator

- (\* ) Piggyback experiment with Tracy Yang (B-3)
- (\* ) Piggyback experiment with Gregory Nelson (B-21)
- (\* ) Piggyback experiment with Betsy Sutherland (B-9)

## **PARTICIPANTS STATISTICS**

<b>PARTICIPANTS</b>	<b>BNL-3</b>
<b>Ph.D., Principal Investigators</b>	<b>22</b>
<b>Ph.D., Co-Principal Investigators</b>	<b>6</b>
<b>Co-Investigator, Investigator</b>	<b>3</b>
<b>Co-Workers</b>	<b>11</b>
<b>Ph.D.</b>	<b>11</b>
<b>Students</b>	<b>2</b>
<b>Post-Doctoral Students</b>	<b>2</b>
<b>Research Associates</b>	<b>4</b>
<b>Research Assistants</b>	<b>1</b>
<b>Assistants</b>	<b>1</b>
<b>Technicians</b>	<b>1</b>
<b>Total:</b>	<b>64</b>

<b>INSTITUTIONS</b>	<b>BNL-3</b>
<b>National</b>	<b>21</b>
<b>International</b>	<b>1</b>
<b>Total</b>	<b>22</b>

## BEAM CHARACTERISTICS

	<sup>56</sup> Fe <sup>26</sup> 600 MeV/n	<sup>56</sup> Fe <sup>26</sup> 1000 MeV/n
<b>Fluence (particles/cm<sup>2</sup>/sec)</b>		
Maximum on target	1.12 x 10 <sup>7</sup>	1.12 x 10 <sup>7</sup>
Minimum on target	5.97 x 10 <sup>3</sup>	4.92 x 10 <sup>3</sup>
<b>Spill rate</b>	<b>30 spills/min</b>	<b>30 spills/min</b>
<b>Spill length</b>	<b>500 msec</b>	<b>500 msec</b>
<b>Particles/spill</b>		
Maximum	3.9 x 10 <sup>8</sup>	4 x 10 <sup>8</sup>
Minimum	2.1 x 10 <sup>6</sup>	1.7 10 <sup>3</sup>
<b>Beam spot diameter</b>	<b>7.5 cm</b>	<b>7.5 cm</b>
<b>Beam cut off length.</b>	<b>&lt;1%</b>	<b>&lt;1%</b>
<b>Actual Energy</b>		
Extracted	610+/-10 MeV/n	1087 MeV/n
On Target	565+/-10 MeV/n	1060 MeV/n
<b>Actual LET</b>	<b>177 keV/μm</b>	<b>148 keV/μm</b>
<b>Dose/rate recorded.</b>		
Maximum	19 Gy/min	16 Gy/min
Minimum	0.1 Gy/min	0.07 Gy/min
<b>Minimum dose exposure</b>	<b>0.05 Gy</b>	<b>0.05 Gy</b>
<b>No of hours for beam characterization and dosimetry</b>	<b>3</b>	<b>24</b>

## RUN DATES

Run dates	Scheduled		Actual	
	Date	Time	Date	Time
Run start	10/17	0800	10/17	1200
Run end	10/23	1300	10/25	0600
Beam tuned into cave	10/16	0800	10/16	1837
Beam delivered to users				
A. Fe 1 GeV/n	10/17	0800	10/17	1200
End run	10/21	0300	10/22	1832
B. Fe 0.6 GeV/n	10/21	1900	10/22	2015
End run	10/23	0900	10/24	2000
C. Fe 1 GeV/n	10/23	2100	10/24	2015
End run	10/23	1300	10/25	0600

## BEAM TIME DESCRIPTION (hours)

Total Clock Time	(from 10/17 1200 to 10/25 0600)	180
Total Beam-on Time	149	
Total Beam-off time	31	
Beam Time for Biology		
1 GeV/n	66	
0.6 GeV/n	16	
Sub-total	82	
Beam Time for Physics		
1 GeV/n	24	
0.6 GeV/n	13	
Sub-total	37	
Beam time for dosimetry, calibration etc.		
1 GeV/n	27	
0.6 GeV/n	3	
Sub-total	30	
Totals	149	

## EXPERIMENTERS AND RUN STATISTICS

Exp. ID	Principal Investigator	Energy	Beam Time Approved	Beam Time Used	Dose Range (cGy)	Dose/Rate (cGy/min)	Number of Samples
B1	Miller	1 GeV	8	14	NA	NA	NA
		600 MeV	16	9			
B2	Chen	1 GeV	2	0.5	NA	NA	NA
B3	Yang	1 GeV	7	7	50 - 500	200	175
		600 MeV	1	1			
B7	Rabin	1 GeV	1.5	6	50 - 200	50 - 100	132
		600 MeV	4.5	-			
B9	Sutherland	1 GeV	2.25	5	35 - 140	100	70
		600 MeV	0.75	2			
B10	Lutze-Mann	1 GeV	6	6	100	30 - 90	102
B12	Hei	1 GeV	4	4	10 - 300	100	136
B13	Kubiczek	1 GeV	3	3	10 - 295	100 - 200	94
		600 MeV	1	2			
B14	Metting	1 GeV	2	2	10 - 80	100	50
B15	Waldren	1 GeV	3.5	1	8 - 200	13 - 74	128
B18	Cooper	1 GeV	2.5+	6	10 - 160	800 - 1500	162
		600 MeV	2.5+	5	Gy		
B19-20	Kronenberg	1 GeV	20+	15	30 - >2000	100 - 1000	150
B21	Nelson	1 GeV	3	3	700 - 7000	1000	44
B22	Vazquez	1 GeV	3	3	5 - 200	50 - 100	392
		600 MeV	1	1			
B23	Brooks	1 GeV	1.25	2	20 - 100	100	20
B24	Borak	1 GeV	5+	11	NA	NA	NA
		600 MeV	5+	4			
B25	Evans	1 GeV	1.5	2	63 - 250	100	30
B26	Morgan	1 GeV	2	2	10 - 1000	200	80
B27	Jorgensen	1 GeV	1	1	1 - 450	1000	23
		600 MeV	3	3	Gy		
B28	Furusawa	1 GeV	NA	NA	200 - 1400	200	14
		600 MeV					
B29	Mohan	1 GeV	0.25	NA	10 - 140	NA	NA
B30	Kale	600 MeV	NA	NA	NA	NA	NA
<b>Totals</b>			<b>113.5 hr.</b>	<b>119 hr.</b>	<b>5 cGy to 450 Gy</b>	<b>13 to 1000 cGy</b>	<b>1802+</b>

## PARTICIPANTS AND BIOLOGICAL SAMPLES

<b>Exp.</b>	<b>Title</b>	<b>Participants</b>	<b>Biological sample</b>
B-2	Radiation Induced Genomic Instability	D. Chen (PI)	Human cell line (reduced expression of Rad51 and hhRad52 genes)
B-3	Effect of Shielding on the Induction of Oncogenic and Cytogenetic Damages	T.C. Yang (PI)	Mouse Fibroblasts (C3H10T1/2) Human Fibroblasts Human Lymphocytes Human mammary epithelial cells Canine kidney cells (MDCK)
B-7	Effects of Exposure to Heavy Particles	B. Rabin (PI)	Rod. Sprague-Dawley
B-9	DNA Damage and Restoration in Mammalian Cells and Tissues	B. Sutherland (PI)	Human skin fibroblast and epithelial cells
B-10	Molecular Analysis of HZE Damage in Transgenic Mice	L. Lutze-Mann (PI)	Transgenic Mice: C57lacZ, CBA1acZ, p53 hemizygous lacZ, p53 nullizygous lacZ
B-12	Cytogenetic and Neoplastic Transforming Effects of heavy Ions in mammalian Cells	T. Hei (PI)	Human epithelial cells: bronchial cells BEP2D and breast cells MCF-1F
B-13	Molecular Damage by 1 GeV/amu Fe-ions	E. B-Kubiczek (PI)	Human cell lines: (MCF7, PC3, WT,ADR AND HCT15)
B-14	Effect of Heavy Ion Exposure on a Mechanism of Cell-Cycle Regulation	N. Metting (PI)	Human skin fibroblasts Human keratinocytes
B-15	HZE Radiation Genotoxicity in Mammalian Cells	C. Waldren (PI)	Human-hamster hybrid cell line (A <sub>L</sub> )
B-18	DNA Repair and early Development of Chromosomal Changes	P. Cooper (PI)	Human fibroblasts (GM38)
B-19	Mutagenesis Studies in Human Cells	A. Kronenberg (PI)	Human lymphoid cells (TK6) WTK-bclX <sub>L</sub>
B-20	High LET Radiation and Genomic Instability in Human Cells	A. Kronenberg (PI)	TK6 cells
B-21	Apoptosis and Oxidative Stress genes Modulate Charged Particle Radiation Damage in the Nematode <i>C. elegans</i>	G. Nelson (PI)	Nematodes (different strains)
B-22	In Vitro Cellular and Molecular Effects of Heavy Ions and Target Fragmentation on Neural Cells	M. Vazquez (PI)	Chick embryos retinal explants
B-23	In Vivo Induction and Repair of Genomic Instability	A. Brooks (PI)	Rat epithelial cells from lungs, trachea and bone marrow.
B-25	Induction of Genomic Instability in Human Lymphoblasts	H. Evans (PI)	Human lymphoblast (TK6 and WTK1)
B-26	Mechanisms of High LET Genomic Instability	W. Morgan (PI)	GM10115 Cell line
B-27	DNA Strand Breaks Produced in Mammalian Cells by Heavy Ion Irradiation	T. Jorgensen (PI)	VC79 Chinese Hamster Cells
B-28	Effects of Shielding on the Induction of Oncogenic and Cytogenic Damages in Mammalian Cells by Energetic Iron Particles	Y. Furusawa (PI)	VC79 Chinese Hamster Cells
B-29	Genetic Effects of Iron Ions	M. Mohan (PI)	Normal human macrophage cells (Mono Mac 6)
B-30	Iron Ion Mutagenesis	P. Kale (PI)	Drosophila Fly